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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,475	01/22/2002	Alexander Gaiger	014058-014402US	3551

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EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,475	GAIGER ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The Election filed 8/22/05 in response to the Office Action of 3/8/05 is acknowledged and has been entered. Applicant elected group IV with traverse.

The traversal is on the ground(s) that a search and examination of all of the inventions would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. The groups outlined in the restriction include distinct polynucleotides, distinct polypeptides, distinct antibodies, distinct methods of detection, distinct cell populations, distinct methods of treatment, and distinct methods of screening. Each method is further unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Searching and examining each of these products and methods would result in a serious burden on the examiner. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim 6 is pending.

Claims 6 is currently under consideration.

Claim Objections

Claim 6 is objected to because of the following informalities: Claim 6 recites "(b) contacting the biological sample with a binding agent that binds to a polypeptide ~~of claim 2~~ encoded by nucleic acid comprising the sequence...." There appears to be an article missing before the word "nucleic". It is suggested that the word "the" is inserted before "nucleic". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites "a predetermined cut-off value" is to be used to determine the presence of cancer in a patient. It is unclear what this pre-determined cut-off value is or how it will be obtained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting the presence of lymphomas in a patient, does not reasonably provide enablement for method for detecting the presence of every type of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Claim 6 is drawn to a method for determining the presence of every *and any type of cancer* in a patient comprising the step of comparing the amount of a polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof in a sample to a predetermined cut-off value.

The specification teaches that the polynucleotide sequence SEQ ID NO:10,582 was identified, using a combination of PCR subtracted cDNA libraries, microarray

analyses, and RealTime PCR, as a gene with a similar tissue expression profile to CD20 and CD52 in lymphomas (Example 5, in particular). The specification further teaches that SEQ ID NO:10,582 is also termed Ly1448 (see Figure 9 and paragraph 576, in particular). The specification further teaches that higher levels of antibodies that interact with a polypeptide encoded by SEQ ID NO:10,582 are present in the sera of lymphoma patients as compared to normal controls (see Figure 31 and Example 13, in particular), which indicates that a polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 could be used as a diagnostic marker for lymphomas. However, the specification does not demonstrate that *a* polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof could be used as a diagnostic marker for *every* type of cancer.

If a molecule such as a protein encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in

prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the peptides in any diagnostic setting without undue experimentation.

The Applicants have presented sufficient data demonstrating that detection of a protein encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 could be used as a diagnostic marker for lymphomas, but the Applicants have not demonstrated that expression of a protein encoded by a nucleic acid

comprising the sequence set forth in SEQ ID NO:10,582 could be used as a marker for any other type of cancer. Further, one of skill in the art would recognize that the lymphomas differ greatly from most other cancers. Lymphomas involve circulating lymphocytes of the lymphatic system; In contrast, the majority of other cancers are carcinomas, which are epithelial in origin. Additionally, etiologies of lymphomas differ from those of other types of cancers, lymphomas require different methods for treatment than other types of cancers, and lymphomas involve methods of detection distinct from other types of cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER